The association between diabetes medication and weight change in a non-surgical weight management intervention: an intervention cohort study

Diabetes medication and weight change in weight management.

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Abstract

Aims: To compare weight change in a lifestyle-based weight management programme between participants taking weight-gaining, weight-neutral/loss and mixed diabetes medications.

Methods: Electronic health records for individuals (≥18 years) with type 2 diabetes who had been referred to a non-surgical weight management programme between February 2008 and May 2014 were studied. Diabetes medications were classified into three categories based on their effect on body weight. In this intervention cohort study, weight change was calculated for participants attending ≥2 sessions.

Results: All 998 individuals who took oral diabetes medications and attended ≥2 sessions of weight management were included. 59.5% were women with a mean BMI of 41.1 kg/m^2 (women) and 40.2 kg/m^2 (men). Of the diabetes medication combinations prescribed, 46.0% were weight-neutral/loss, 41.3% mixed and 12.7% weight-gaining. The mean weight change for participants on weight-gaining and weight-neutral/loss diabetes medications respectively was -2.5 kg (95% CI: -3.2 to -1.8 kg) and -3.3 kg (95% CI: -3.8 to -2.9 kg) (p = 0.05) for those attending ≥2 sessions (n = 998). Compared to those prescribed weight neutral medications, those prescribed weight gaining medication lost 0.86kg less (95% CI: 0.02 to 1.7 kg; p=0.045) in a model adjusted for age, sex, BMI and socioeconomic status.

Conclusions: Participants on weight-neutral/loss diabetes medications had a greater absolute weight loss within a weight management intervention compared with those on weight-gaining medications. Diabetes medications should be reviewed ahead of planned weight-loss interventions to help ensure maximal effectiveness of the intervention.

Keywords

Weight control, type 2 diabetes, observational study, database research, obesity therapy.

What's new?

- In many oral diabetes medications are associated with weight gain, which makes the management of type 2 diabetes in individuals with overweight and obesity more challenging.
- There was a clinically significant larger weight loss in individuals on weight-neutral/ loss diabetes medication compared to those on weight-gaining medication**.**
- There is a gradated relationship between greater use of weight-gaining diabetes medication and lower success of a weight-loss programme.
- Diabetes medication regimens should be reviewed prior to referral to a weight management programme to ensure that, when possible, weight neutral/ loss medications are used preferentially over weight-gaining medications.

Introduction

Obesity is the major risk factor for the development type 2 diabetes mellitus (Type 2 DM) and 87.2% of people living with Type 2 DM have a body mass index (BMI) in the overweight or obese range [1]. Weight gain and obesity increases the likelihood of developing Type 2 DM [2], therefore weight loss is a key therapeutic goal in the management of Type 2 DM [3]. National Institute of Clinical Excellence (NICE) [4] and the American Diabetes Association (ADA) guidelines [5] recommend that people with obesity and Type 2 DM should have individualised interventions, including behavioural interventions, pharmacotherapy or surgery to promote weight loss, in order to improve glycaemic control. However there is no guidance given on how to manage the treatment of Type 2 DM around the time of a weight management programme.

Many diabetes medications are associated with weight gain [6]. Therefore, the ADA and the European Society for the Study of Diabetes (EASD) have developed an algorithm for hyperglycaemia management in Type 2 DM where individuals who have a BMI in the overweight or obese range should be initially prescribed diabetes medication that either contributes to weight reduction or does not have an effect on weight [3]. They recommend that metformin be used first-line for people with Type 2 DM with a body mass within the normal, overweight or obese range. If metformin proves inefficient in regulating glycaemia, or is contraindicated for individuals with overweight or obesity, then glucagon-like peptide-1(GLP-1 receptor) agonists, sodium-glucose co-transporter-2 (SGLT2) inhibitors, and dipeptidylpeptidase-4 (DPP-4) inhibitors should be considered as these are associated with weight reduction [3].

Sulfonylureas and thiazolidinediones are known to cause weight gain. The United Kingdom Prospective Diabetes Study (UKPDS) suggests that sulfonylureas can cause 5kg weight gain over a 10-year period of treatment [7]. In addition, in the PROACTIVE trial, the thiazolidinediones pioglitazone produced an average of 3.6 kg weight gain over three years [8]. Conversely, 27 randomised controlled trials (RCTs) show that GLP-1 receptor agonists were associated with significant weight reduction and a mean weight loss of -1.74 kg [9]. A significant reduction in body weight was recorded in a 52-week study, in which the SGLT2 inhibitor empagliflozin was added to insulin treatment for people who have obesity with uncontrolled diabetes [10].

While some diabetes medications can lead to weight gain, there is currently no evidence as to the effect of these same medications on the ability of an individual to intentionally lose weight within a weight management programme. There is evidence that those with Type 2 DM achieve lower weight loss within these programmes than those without diabetes, and medications have been suggested as a contributory factor [11]. There have been no studies examining the outcomes of weight management by diabetes medication class. The aim and novelty of this study is to compare weight changes in a lifestyle-based weight management programme between participants taking weight-gaining, weight-neutral and mixed diabetes medications.

Methods

Study procedure

This study uses data from electronic health records from the Glasgow and Clyde Weight Management Service (GCWMS), based in Glasgow, United Kingdom. The service is part of the National Health Service and is accessible to people aged 18 years and over with complex obesity (defined as BMI ≥30 kg/m^2 with obesity-related comorbidities, or BMI ≥35 kg/m^2), who have been referred by a GP or hospital doctor. The goal of the service is to support people to achieve weight losses of at least 5 kg.

The GCWMS intervention studied here, predominately delivered in group settings, consists of diet (600 kcal deficit diet), exercise and behavioural advice over nine sessions (90 min), delivered once every two weeks over a 16-week period. Personalised dietary prescriptions are calculated based on the participant's age and sex. Sessions involve semi-structured dietician led presentations and group discussion to encourage lifestyle change and healthy eating based on the Eatwell Plate [12] and behaviour change approaches. Supplementary exercise sessions (weekly group based; physiotherapy led), psychological talks/seminars (self-help advice), and more intensive 1:1 or group psychological therapy may be offered.

Diabetes medication classification

Diabetes medications were classified into seven groups: biguanides, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, thiazolidinediones, sulfonylureas and insulin. Brand names in addition to any combined medications available in the UK were identified using the British National Formulary (BNF) 2016 [13]. Using data from RCTs [9, 14, 15, 16], the medications were then categorised according to their effect on body weight (combination

medications were categorised by their individual components) as weight-neutral/loss, or weight-gaining. Three groups were formed:

1. Weight neutral/loss medications:
Metformin only or Metformin +DPP-4 +/OR GLP-1 +/OR SGLT2

2. Mixed weight effect medications:
(Sulfonylureas) AND (Metformin +/OR DPP-4 +/OR GLP-1 +/OR SGLT2)
or **(Thiazolidinediones + sulfonylureas) OR (TZDs)** AND (Metformin +/OR DPP-4 +/OR GLP-1 +/OR SGLT2)

3. Weight gaining medications:
Sulfonylureas only or sulfonylureas + thiazolidinediones or any combination including insulin

Data source, inclusion and exclusion criteria

At referral, all medications were imported into the GCWMS database from the Scottish Care Information (SCI) gateway referral. This is an electronic referral system that transmits prescription information from the general practice IT system. Current prescriptions at time of participant's referral were evaluated. Search terms were used to ascertain the diabetes medications used for classification and coding according to the BNF [13]. Participants aged ≥18 years, referred to GCWMS between 1/1/2008 and 31/12/2014, prescribed diabetes medications and attending ≥2 sessions in the lifestyle phase were included. If the same person was referred more than once, information from the earliest referral only was included [17, 18]. Type 2 diabetes status was determined from either mention on the primary care referral form or at assessment visit. Each person was assigned to one category of medication as described above, and any person on insulin only or on any combination not described above was excluded. Initial numbers in each drug group, mean BMI, BMI categories, sex, the Scottish Index of Multiple Deprivation (SIMD) and age were identified. The SIMD score is calculated from information on seven domains (current income, employment, health, education, skills and training, geographic access to services, housing, and crime) to describe the level of deprivation in small geographic areas (6,505 data zones) across Scotland. The SIMD is used to derive quintiles of socioeconomic status for the Scottish population, ranging from 1 (most deprived) to 5 (least deprived). Prior to analysis, programme completion was defined as completion of the programme with attendance at 80% of the sessions; i.e. ≥seven sessions attended out of a possible nine. This analysis was conducted by employees of the Health Board as part of a wider service evaluation using an anonymised dataset. All

participants had given written consent for the use of their data for service evaluation and research purposes, and written permission for this analysis was granted by the GCWMS Operational Research Committee.

Statistical methods

The results are reported as number, mean and percentages. The differences in participant characteristics, such as mean age and BMI, were tested using an independent samples t-test. A Chi-square test for trend was used to test differences in ordinal variables. Differences in mean weight change and mean percentage weight change were analysed using two-way t-test (between two groups) and ANOVA (more than two groups) for continuous data. The Bonferroni (pairwise) test was used to adjust for multiple comparisons. Statistical significance was defined as p <0.01 in the case of multiple comparisons, and p <0.05 up to two pair comparisons. All statistical analyses were performed using Stata version 12.1 (StataCorp, College Station, Texas). A stratified analysis was also conducted to allow visualisation of the potential confounding factors. Finally, to minimise the effect of potential confounding factors, such as initial BMI, sex and age, a multivariable regression was conducted adjust for age, sex, baseline BMI group and SIMD.

Results

Baseline characteristics

In total, 998 individuals with Type 2 DM attended ≥2 sessions of weight management at GCWMS and 560 completed the programme (59.5% women). 46.0%, 41.3% and 12.7% of those included were on weight-neutral/loss, mixed and weight-gaining diabetes medications respectively. Compared to those prescribed weight-gaining medications, those prescribed weight-neutral medications had a higher mean BMI (BMI 42.3 kg/m^2 [95% CI: 41.6 to 43.0 kg/m^2] vs 40.8 kg/m^2 [95% CI: 39.7 to 42.0 kg/m^2]; p = 0.037) and were younger (mean ages were 52.1 years [95% CI: 51.0 to 53.3 years] and 58.2 years [95% CI: 56.3 to 60.2 years], respectively; p = 0.001).

Table 1 shows the baseline characteristics of the included population by medication group. A lower proportion (9.8%) of individuals with higher BMIs were prescribed weight-gaining medications (p = 0.19). Additionally, a higher proportion of older people (≥50 years) were prescribed weight-gaining medications, than younger people (p = 0.001). Moreover, a higher proportion of women were prescribed weight-neutral/loss medications (50.0%) than men (40.1%) (p = 0.002). There was no association between SIMD and medication prescribing (p = 0.08, 0.34 and 0.41).

Weight loss outcomes

There is a gradated relationship between greater use of weight-gaining diabetes medication and lower success of a weight-loss programme. By the end of the lifestyle programme (16 weeks), participants prescribed weight-neutral/loss medications (n=248) who completed the programme had a greater absolute weight loss than those prescribed weight-gaining medications (n=76); mean weight changes were -4.9 kg (95% CI: -5.5 to -4.2 kg) and -3.3 kg (95% CI: -4.2 to -2.5 kg, p = 0.005), respectively (Table 2, Figure 1). The difference in percentage weight change between the two groups (-4.1% [95% CI: -4.6 to -3.6%] vs -3.2% [95% CI: -4.0 to -2.4%]) did not reach statistical significance (p = 0.06). The mean weight change for patients on mixed medications who completed the programme was -4.3 kg (95% CI: -4.8 to -3.8 kg). Accounting for the total group, including those who did not complete the programme, weight loss was -3.3 kg (95% CI: -3.8 to -2.9 kg) in the weight-neutral/loss medication group and -2.5 kg (95% CI: -3.2 to -1.8 kg) in the weight-gaining medication group (p = 0.05).

There were no significant differences between the participants, neither completers nor the whole cohort, prescribed weight-neutral/loss medications and those prescribed mixed drugs in terms of mean change in weight or percentage of weight loss (p = 0.73 and 0.98, respectively). However, the difference in weight change among completers was between the weight-neutral/loss and weight-gaining groups (p=0.005) and suggests a gradated relationship.

Weight loss outcomes by baseline characteristics

To explore if the effect of differences in baseline characteristics between groups a stratified analysis (Table 3) and multivariate regression (supp table 1) was conducted. The mean weight change when prescribed weight-neutral/loss medications was -3.93 kg (95% CI: -4.7 to -3.0 kg) for men and -2.98 kg (95% CI: -3.4 to -2.5 kg) for women, (p = 0.02 for difference between sexes) (Table 3). Men made up a higher proportion of the group prescribed mixed medications (45.4%), and women made up a higher proportion of those prescribed weight neutral/loss medications (64.6%). There was no significant weight change between men and women prescribed mixed-effects medications (mean change in men and women was -3.32 kg (95% CI: -3.8 to -2.8 kg) and -3.12 kg (95% CI: -3.6 to -2.5 kg), p = 0.59, respectively). There was no difference in the mean weight loss between men and women prescribed weight-gaining medications (p = 0.98). Weight loss among those prescribed weight-neutral/loss, mixed or weight-gaining diabetes medications did not vary by BMI, age, or socio-economic deprivation category (SIMD) (all p>0.05). Examining the total cohort (those attending ≥ 2 sessions; n=998), there was 0.86kg less weight loss (95% CI: 0.02 to 1.7 kg; p = 0.045) in those prescribed weight gaining medications compared to those on weight neutral/ loss medications, in a model adjusted for age, sex, BMI group and socio-economic deprivation category (SIMD).

Discussion

Among all participants prescribed diabetes medications, we found that a lifestyle-based weight loss programme was less effective for people prescribed weight-gaining medications. The objective of this research was to study the relationship between prescribed diabetes medications and subsequent weight loss within a weight management intervention. Weight loss is essential for diabetes management as glycaemic control and cardiovascular risk factors improve with 5-10% weight loss [19]. Despite it being well known that diabetes medications can affect body weight, this is the only study to our knowledge to report the effects of these medications on intentional weight loss outcomes, an area of increasing interest in the treatment of Type 2 DM [20]. Participants who were prescribed weight-gaining diabetes medications lost less weight than those on weight-neutral/loss medications, with a 0.86 kg difference between groups in a model adjusting for potential confounding factors. This difference is clinically significant in the context of weight management for reducing the risk of complications.

46.0%, 41.3% and 12.7% of the included participants were on weight-neutral/loss, mixed and weight-gaining diabetes medication respectively. This is consistent with DiaRegis cohort study, a real-world study of 3,807 people with Type 2 DM in Germany, which found that people with lower BMI were more likely to be prescribed SUs or insulin, while people with higher BMI were more likely to be prescribed biguanides or GLP-1 receptor agonists [21]. We found that weight-neutral/loss medications were prescribed more frequently for younger people, consistent with a previous study by Ewenighi *et al* [22], which found that only age and initial BMI influenced the prescribing of diabetes medications.

There was a difference in mean weight loss between men and women who were prescribed weight-neutral/loss medications, however a lower proportion of men were prescribed weight-neutral medications compared to other medications. However, men who were prescribed weight-neutral medications lost the largest amount of weight meaning the relationship between medication type and weight loss was not wholly confounded by sex. A previous 26-week RCT compared the effect of liraglutide or rosiglitazone with glimepiride on weight change and glycaemic control in 1,041 participants. It reported that sex does not influence the effect of liraglutide on weight change, which is consistent with the current results [23]. In addition, in a two-year follow up of the DiaRegis cohort study, Hartmann *et al*. found that the association between diabetes medications and weight change was not influenced by the sex or age of participant [21].

The difference in weight loss achieved across the three medication groups was in keeping with the known effects of these medications on body weight, when prescribed without the addition of a lifestyle weight management intervention. For instance, an earlier study (1-year duration) of 639 individuals with Type 2 DM showed that participants who received sulfonylureas plus thiazolidinediones gained an average of 2.8 kg, compared with a reduction of 1 kg in those prescribed metformin plus sulfonylureas [24]. In addition, a four-year randomised study of 4,360 participants with Type 2 DM uncontrolled by lifestyle intervention and treated with metformin, rosiglitazone or glibenclamide showed individuals in the metformin group lost weight, with weight gain in the glibenclamide and rosiglitazone groups; this difference was greatest between the metformin and the rosiglitazone group [25]. Moreover, a retrospective study (1-year duration) of 2,641 participants reported that people on metformin had lost an average weight of -2.6 kg (95% CI: -2.5 to -2.9 kg), and those on sulfonylureas had gained 0.3 kg (95% CI: -0.2 to 0.8 kg) [26].

The beneficial effects of weight loss on glycaemic control and minimizing the number of diabetes medications used by people with diabetes are now established [27, 28], as are the weight gaining effects of commonly used diabetes medications. Failure to lose weight early within a weight management intervention is associated with nonattendance and disengagement [29], leading to poor weight loss outcomes. It is therefore vital that a review of person's medications is conducted before commencing a weight management intervention and where possible prescribing people with alternative medications that are not associated with weight gain without compromising glycaemic control.

Strengths and limitations

The main strength of this research is the unique large dataset available, derived from one of the largest weight management programmes in the United Kingdom, providing objective measures of weight and height. The gradated relationship, showing intermediate weight changes among participants prescribed mixed-effect medications, strengthens the observation that the relationship may be causal. To the best of our knowledge, this is the only study to observe the association between diabetes medications and weight change for individuals with obesity and Type 2 DM (the included participants had a BMI of $\geq$30 kg/m^2). There was potential prescribing bias due to people being prescribed their medication based on age and weight. Selection bias was minimal, with only 1.8% of participants excluded (on account of their being on drug regimens that could not be classified into one of the groups). The prescribing information is likely to be accurate, as all data were sourced from electronic prescription records. The main weakness of this study was the lack of comorbidity

information, the lack of information on the participants' duration of Type 2 DM and how long they had been prescribed the medications, which may have influenced their effect; however duration and age are likely closely related and age did not confound the relationship. In addition, it is possible that prescribed the medications may have changed between referral and starting the programme, but the likelihood of this is considered low given the short time between referral and starting the programme.

Conclusions

Individuals prescribed weight-neutral/loss diabetes medications had a greater absolute weight loss within a weight management intervention compared with those prescribed weight-gaining medications. While those prescribed weight neutral medications had a higher BMI on average than those on weight gaining medications, there were many prescribed weight gaining medications that were deemed in need of weight management. Ensuring that people are prescribed appropriate diabetes medications at the time of referral to a lifestyle weight management programme may help maximise the success of the intervention. Future studies to assess the long-term effects of diabetes medications on weight loss maintenance and glycaemic control during weight loss will help clarify clinical guidance in this important area.

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Competing of interest: JL is leading a Joint Working Agreement between NHS Greater Glasgow and Clyde, University of Glasgow, Astra Zeneca and MSD, to develop educational materials for primary on weight management in people with Type 2 DM. She has received an unrestricted grant from Janssen for the same project.

Author contributions: JL, NMA and DSM designed the study. NMA, PM and BS carried and interpretation of data, and statistical analyses. NMA, JL and DSM contributed to interpreting the results; NMA drafted the initial manuscript. JL, NMA, DSM, HK, BS, PM, RS and SM revised and finalised the manuscript. All the authors approved the final manuscript.

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TABLE 1 Baseline characteristics of people referred to GCWMS with Type 2 DM.

	All participants included (attended ≥2 session) *N*=998	Weight-neutral medications *n*=459 (46%)	*p*	Mixed medications *n*=412 (41.3%)	*p*	Weight-gaining medications *n*=127 (12.7%)	*p*
	N(% of total cohort)	*n(% of total subgroup)*					
Sex							
Men	404 (40.5)	162 (40.1)	0.002	187 (46.3)	0.008	55 (13.6)	0.48
Women	594 (59.5)	297 (50.0)		225 (37.9)		72 (12.1)	
Not known							
Initial BMI (kg/m^2)							
30–34.9	170 (17.0)	70 (41.2)	0.07	71(41.8)	0.52	29 (17.1)	0.19
35–39.9	289 (29.0)	121 (41.9)		129 (44.3)		39 (13.5)	
40–49.9	427 (42.8)	210 (49.2)		169 (39.6)		48 (11.2)	
≥50	112 (11.2)	58 (51.8)		43 (38.4)		11(9.8)	
Age (years)							
18–29	24 (2.4)	20 (83.3)	0.001	2 (8.3)	0.001	2 (8.3)	0.08
30–39	78 (7.8)	56 (71.8)		16 (20.5)		6 (7.7)	
40–49	186 (18.6)	105 (56.5)		64 (34.4)		17(9.1)	
50–59	330 (33.1)	142 (43.0)		149 (45.2)		39 (11.8)	
60–69	289 (29.0)	105 (36.3)		136 (47.1)		48 (16.6)	
≥70	91 (9.1)	31 (34.1)		45 (49.4)		15 (16.5)	
SIMD							
Most deprived	396 (39.7)	191 (48.2)	0.08	157 (39.6)	0.34	48 (12.1)	0.41
2	202 (20.2)	98 (48.5)		78 (38.6)		26 (12.9)	
3	146 (14.6)	64 (43.8)		60 (41.1)		22 (15.1)	
4	124 (12.4)	43 (34.7)		61 (49.2)		20 (15.9)	
Least deprived	126 (12.6)	60 (47.6)		55 (43.7)		11(8.7)	
Not known	4 (0.4)	3 (75.0)		1 (25.0)		0	

Abbreviations: GCWMS, Glasgow and Clyde Weight Management Services; Type 2 DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; SIMD, Scottish Index of Multiple Deprivation; N, number. (P-value <0.01 considered statistically significant).

TABLE 2 Weight loss outcomes for people with Type 2 DM receiving different categories of diabetes medication.

Drugs categories	n (Total =998)	%	Mean weight change and 95% CI (kg)	*p*-value (completers) (groups compared)	*p*-value (total) (groups compared)	Mean % weight change and 95% CI	*p*-value (completers) (groups compared)	*p*-value (total) (groups compared)
1- Weight-neutral medications								
Completers (≥7 sessions)	248	54.0	-4.9 (-5.5 to -4.2)			-4.1 (-4.6 to -3.6)		
Non-completers (<7 sessions)	211	46.0	-1.4 (-1.8 to -1.0)					
Total (≥2 sessions)	459		-3.3 (-3.8 to -2.9)			-2.8 (-3.1 to -2.5)		
2- Mixed medications				1 vs 2 **0.14**	1 vs 2 **0.73**		1 vs 2 **0.31**	1 vs 2 **0.98**
Completers (≥7 sessions)	236	57.2	-4.3 (-4.8 to -3.8)			3.8 (-4.2 to -3.3)		
Non-completers (<7 sessions)	176	42.7	-1.7 (-2.2 to 1.2)					
Total (≥2 sessions)	412		-3.2 (-3.5 to -2.8)			-2.8 (-3.1 to -2.4)		
3- Weight-gaining medications				1 vs 3 **0.005**	1 vs 3 **0.05**		1 vs 3 **0.06**	1 vs 3 **0.17**
Completers (≥7 sessions)	76	59.8	-3.3 (-4.2 to -2.5)			-3.2 (-4.0 to -2.4)		
Non-completers (<7 sessions)	51	40.1	-1.1 (-2.2 to -0.9)					
Total (≥2 sessions)	127		-2.5 (-3.2 to -1.8)			-2.3 (-2.9 to -1.7)		

Abbereviations: N, Number; CI, Confidence Interval. (P-value <0.05 considered statistically significant). The difference in weight change among completers (attended ≥7 session) was between the weight-neutral/loss and weight-gaining groups (p=0.005). However, there was no difference in case of percentage weight change.

TABLE 3 Stratified analysis of weight loss with three different categories of diabetes medications at end of the lifestyle phase in completers and non-completers.

	Weight-neutral medications (n = 459)			**Mixed medications (n = 412)**			**Weight-gaining medications (n = 127)**		
Category (n)	**Mean weight change (kg) and (95% CI)**	**n (%)**	***P***	**Mean weight change (kg) and (95% CI)**	**n (%)**	***P***	**Mean weight change (kg) and (95% CI)**	**n (%)**	***P***
Men (404)	-3.93 (-4.7 to -3.0)	163 (35.5)	0.02	-3.32 (-3.8 to -2.8)	187 (45.4)	0.59	-2.51 (-3.7 to -1.2)	55 (43.3)	0.98
Women (594)	-2.98 (-3.4 to -2.5)	296 (64.5)		-3.12 (-3.6 to -2.5)	225 (54.6)		-2.50 (-3.2 to -1.7)	72 (56.7)	
BMI 30–34.9 kg/m^2 (179)	-2.48 (-3.2 to -1.6)	70 (15.3)	0.08	-2.80 (-3.4 to -2.1)	71 (17.2)	0.27	-2.86 (-3.9 to -1.7)	29 (22.8)	0.84
BMI 35–39.9 kg/m^2 (301)	-2.82 (-3.5 to -2.0)	121 (26.4)		-2.83 (-3.3 to -2.3)	129 (31.3)		-2.04 (-3.4 to -0.5)	39 (30.7)	
BMI 40–49.9 kg/m^2 (414)	-3.68 (-4.3 to -3.0)	210 (45.7)		-3.5 (-4.2 to -2.8)	169 (41.0)		-2.61 (-3.8 to -1.4)	48 (37.8)	
BMI ≥50 kg/m^2 (104)	-3.98 (-5.0 to -2.9)	58 (12.6)		-3.70 (-5.3 to -2.0)	43 (10.4)		-2.72 (-4.7 to -0.7)	11 (8.7)	
Age 18–29 years (24)	-2.01 (-3.6 to -0.3)	20 (4.4)		-1.69 (-4.6 to 1.2)	2 (0.5)		-0.29 (-1.6 to 1.0)	2 (1.6)	
30–39 years (78)	-2.66 (-3.7 to -1.6)	56 (12.2)	0.55	-1.72 (-2.8 to -0.6)	16 (3.9)	0.44	-3.98 (-6.9 to -0.9)	6 (4.7)	0.55
40–49 years (186)	-3.54 (-4.4 to -2.6)	105 (22.9)		-2.79 (-3.5 to -2.0)	64 (15.5)		-2.31 (-3.8 to -0.8)	17 (13.4)	
50–59 years (330)	-3.64 (-4.4 to -2.8)	142 (30.9)		-3.13 (-3.7 to -2.4)	149 (36.2)		-2.45 (-3.8 to -1.0)	39 (30.7)	
60–69 years (289)	-3.2 (-4.1 to -2.3)	105 (22.9)		-3.48 (-4.1 to -2.8)	136 (33.0)		-3.02 (-4.2 to -1.8)	48 (37.8)	
≥70 years (91)	-3.00 (-4.6 to -1.4)	31 (6.7)		-3.75 (-5.2 to -2.2)	45 (10.9)		-1.20 (-2.7 to 0.3)	15 (11.8)	
SIMD: 1 (most deprived) (396)	-2.92 (-3.5 to -2.2)	191 (41.9)		-3.04 (-3.6 to -2.4)	157 (38.2)		-2.71 (-3.6 to -1.7)	48 (37.8)	
2 (202)	-3.28 (-4.0 to -2.5)	98 (21.5)	0.39	-2.78 (-3.5 to -1.9)	78 (19.0)	0.45	-1.86 (-3.6 to -0.7)	26 (20.5)	0.15
3 (146)	-3.85 (-4.9 to -2.7)	64 (14.0)		-3.67 (-5.0 to -2.3)	60 (14.6)		-1.10 (-2.4 to 0.2)	22 (17.3)	
4 (124)	-3.05 (-4.5 to -1.5)	43 (9.4)		-3.1 (-4.0 to -2.2)	61 (14.8)		-3.48 (-5.2 to -1.0)	20 (15.7)	
5 (least deprived) (126)	-4.05 (-5.3 to -2.7)	60 (13.2)		-3.88 (-4.9 to -2.8)	55 (13.4)		-4.14 (-7.2 to -1.0)	11 (8.7)	

Abbreviations: n, number; CI, Confidence Interval, BMI, Body Mass Index; SIMD, Scottish Index of Multiple Deprivation.

Supplementary table:

SUPPLEMENTARY TABLE 1 Multivariable regression of weight change (kg) with baseline characteristics.

Baseline characteristics		Coefficient	95%CI	p-value
Drug group	neutral	0		
	mixed	0.21	(-0.37, 0.79)	0.47
	weight gaining	0.86	(0.02, 1.70)	0.045
Sex	women	0		
	men	-0.40	(-0.94, 0.14)	0.14
Age group (years)	<40	0		
	40-49	-0.72	(-1.74, 0.30)	0.17
	50-59	-0.86	(-1.82, 0.10)	0.08
	60-79	-1.09	(-2.08, -0.10)	0.032
	70+	-0.76	(-2.00, 0.47)	0.23
BMI group (kg/m^2)	<35	0		
	35-<40	-0.35	(-1.13, 0.43)	0.38
	40-<45	-0.55	(-1.36, 0.25)	0.18
	45-<50	-1.06	(-2.00, -0.13)	0.026
	50+	-1.00	(-2.04, 0.05)	0.06
SIMD quintile	1	0		
	2	0.01	(-0.70, 0.73)	0.97
	3	-0.45	(-1.26, 0.35)	0.27
	4	-0.26	(-1.11, 0.60)	0.56
	5	-0.98	(-1.83, -0.12)	0.026
Constant		-1.66	(-2.76, -0.57)	0.00

Coefficients represent difference in change in weight (kg) compared to reference category
+ values indicate less weight loss, - values indicate more weight loss.

CI, Confidence Interval, BMI, Body Mass Index; SIMD, Scottish Index of Multiple Deprivation.

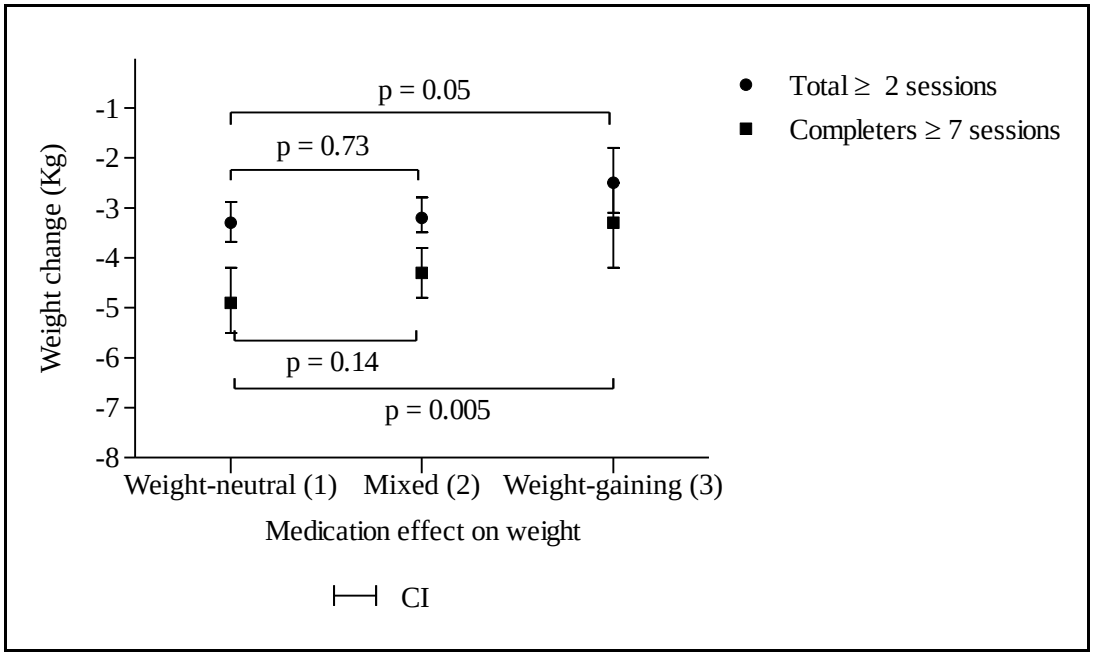

FIGURE 1 The mean weight change (kg) and the 95% confidence intervals (CI) at the end of the lifestyle programme for three different diabetes medication categories. Total completers, n=560 (≥7 sessions; p = 0.14, between groups 1 and 2; p = 0.005, between groups 1 and 3). Total participants including non-completers, n=998 (≥2 sessions; p = 0.73, between groups 1 and 2; p = 0.05, between groups 1 and 3).